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A Psychophysiologic Study of Weakening Traumatic Combat Memories  
With Post-Reactivation Propranolol

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<b>14. ABSTRACT</b>  We have successfully studied 11 subjects as of the end of this report period. The study medication code has not been broken. Hence, there are no findings yet.					
<b>15. SUBJECT TERMS</b> Stress disorders, post-traumatic; reconsolidation; propranolol; imagery, psychotherapy; psychophysiology (all MeSH terms)					
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## INTRODUCTION:

The objective of this project is to test whether the  $\beta$ -adrenergic blocker propranolol, given following combat memory reactivation, results in a significantly greater weakening of traumatic memories than propranolol alone, supporting the proposition that this weakening is due to pharmacological blockade of memory reconsolidation, rather than non-specific actions of propranolol. We hypothesize that subjects who undergo script preparation for the combat event(s) that caused their PTSD, followed by (post-reactivation) propranolol, will show significantly smaller psychophysiologic responses during script-driven imagery testing a week later, indicative of weakening of the emotional memory, compared to those who receive (non-reactivation) propranolol two days prior to combat script preparation. Subjects will be randomly assigned to one of two groups: post-reactivation propranolol or non-reactivation propranolol. Subjects randomized to the non-reactivation propranolol group will receive a “test” dose of propranolol, whereas subjects randomized to the post-reactivation propranolol group will receive placebo. Two days later, all subjects will return for an approximate 15-30 minute “script preparation” session, at which time they will describe the details of their traumatic combat event(s). Subjects randomized to the post-reactivation propranolol group will then receive propranolol, whereas subjects randomized to the non-reactivation propranolol group will receive placebo. Scripts will be composed portraying each subject’s personal combat events in their own words. Subjects will return to the psychophysiology laboratory one week and six months later. During each of these visits, heart rate, skin conductance, and corrugator electromyogram responses during will be recorded during script-driven imagery of personal combat events. The hypothesis predicts that at each time period, the physiologic responses of the post-reactivation propranolol group will be significantly smaller than those of the non-reactivation propranolol group.

## BODY:

After a prolonged process that entailed obtaining IRB approval from the Massachusetts General Hospital, the Department of Veterans Affairs, and the USAMRMC Office of Research Protections (ORP), the PI finally received approval to begin recruiting subjects on March 10, 2008. i.e., 10.5 months after the project’s start date. The lengthy time it took to gain this approval was outside the PI’s control. An extra month was required to implement the recruitment procedures, which could not begin until final ORP approval had been obtained.

Thus, we have now had 12.5 months to recruit subjects. The Statement of Work calls for a recruitment rate of approximately 1.67 subjects per month. According to this rate, the project should have been able to recruit 21 subjects during this period. In actuality, we have succeeded in recruiting and successfully running 11 subjects through the procedure; one additional subject dropped out prior to psychophysiological testing. Hence, our recruitment rate has been 57% of that projected.

In order to address the recruitment problem, we devised the following strategy after obtaining approval from the DOD project officer. We have now cut our annual expenses in half by

reducing staff time and subject participation fees. This will allow us to convert from a three-year to a four-year study, affording an extra year for subject recruitment.

#### KEY RESEARCH ACCOMPLISHMENTS:

In each instance except the one subject that dropped out, the procedure went as planned, and usable data were obtained in all remaining subjects.

#### REPORTABLE OUTCOMES:

The medication code will not be broken until the conclusion of the study. Hence there are not yet any reportable outcomes, and there is not expected to be any until the study's conclusion and data analysis.

#### CONCLUSION:

None yet

#### REFERENCES

None

#### APPENDICES/SUPPORTING DATA:

The table in the next page presents the data obtained in subjects to date.

Key for Table:

VAMC=Studied at Manchester, NH VA Medical Center; MGH=Studied at Massachusetts General Hospital

CAPS: Pre-intervention total score on Clinician-Administered PTSD Scale

Other Axis I: Current comorbid mental disorders

Pprb\_8\_sq: Physiological posterior probability (square-root transformed). This is the study's primary outcome measure. It represents a composite of the four individual psychophysiological responses during script-driven imagery of the traumatic event at Day 8 (i.e., one week after script preparation accompanied by either propranolol or placebo). The four individual measures are: MNSC=mean skin conductance response, MNHR=mean heart rate response, MNCOR=mean corrugators electromyogram response; MNFR=mean frontalis electromyogram response.

Subject #	Study Location	Age	Race	Sex	CAPS	Other Axis I	PPrb_8_sq	MNSC_8	MNHR_8	MNCOR_8	MNFR_8
1	VAMC	56	White, non-Hispanic	M	85	None			Dropped out		
2	VAMC	47	White, non-Hispanic	M	68	GAD	0.25	0.78	-2.86	-0.13	0.02
3	VAMC	25	White, non-Hispanic	M	52	None	0.2	0.00	2.21	-0.75	0.66
4	VAMC	32	White, non-Hispanic	M	65	Major Depression	0.55	0.53	2.06	0.97	0.27
5	VAMC	26	White, non-Hispanic	M	55	Depression, OCDP	0.28	0.05	2.81	-0.37	-0.48
6	VAMC	24	White, non-Hispanic	M	60	None	0.88	3.37	14.04	0.72	-0.01
7	MGH	64	White, non-Hispanic	M	12	None	0.06	-0.34	-1.54	-0.49	0.50
8	MGH	27	White, non-Hispanic	M	68	None	0.46	0.36	2.16	0.24	-0.04
9	MGH	24	White, non-Hispanic	M	81	Panic Disorder, Simple Phobia, Social Phobia, Bipolar Affective Disorder	0.25	0.10	-0.46	0.14	0.13
10	MGH	56	White, non-Hispanic	M	42	Panic Disorder, Simple Phobia, Major Depression	0.25	0.05	0.48	-0.09	-0.08
11	MGH	59	White, non-Hispanic	M	68	None	0.22	0.09	-0.11	-0.05	0.37
12	MGH	45	White, non-Hispanic	M	45	Major Depression, Dysthymia	0.84	2.53	.	1.78	0.34